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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte KENNETH ELIOT SHERMAN

Appeal 2009-009125
Application 09/544,108
Technology Center 1600

Decided: December 2, 2009

Before LORA M. GREEN, RICHARD M. LEBOVITZ, and
JEFFREY N. FREDMAN, *Administrative Patent Judges.*

FREDMAN, *Administrative Patent Judge.*

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving a claim to a method for treating Hepatitis C virus infections. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

Statement of the Case

Background

"Chronic hepatitis develops in at least half the patients with acute HCV infection" (Spec. 2, ll. 4-5). According to the Specification, the "effects of recombinant human interferon α in a prospective, randomized, double-blind, placebo- controlled trial in patients with well-documented chronic HCV infection has recently been carried out" (Spec. 4, ll. 18-21). The Specification teaches that the "authors concluded that interferon α therapy is beneficial in reducing disease activity in chronic hepatitis C; however, the beneficial responses are often transient" (Spec. 5, ll. 12-15).

The Specification also teaches that "[a]nother class of polypeptide immune modifiers derived from the thymus gland, the thymosins, has been shown . . . to augment T-cell function" (Spec. 7, ll. 20-23). According to the Specification, "THNα_1 [thymosin-alpha], has potent immunologic activity, including stimulation of α - and γ-interferon production" (Spec. 8, ll. 16-17).

The Claims

Claims 1, 3-6, and 25 are on appeal. Claim 1 is representative and reads as follows:

> 1. A method of treating a mammal infected with Hepatitis C virus, comprising administering to said mammal an anti-Hepatitis C viral effective amount of at least one α-interferon, concurrently or sequentially with administering a thymosin-α or fragment of thymosin-α.

The prior art

The Examiner relies on the following prior art references to show unpatentability:

Moody US 5,273,963 Dec. 28, 1993

Huang et al., *Follow-up Observation on the Antiviral Effect of Combined Treatment of Small Dosage of Interferon and Thymosin in Patients with Chronic Hepatitis B*, 5 VIROLOGICA SINICA 69-73 (pages 1-12 in translation) (1990).

Hoofnagle et al., *Treatment of Chronic Type C Hepatitis with Alpha Interferon*, 9(4) SEMINARS IN LIVER DISEASE 259-263 (1989).

The issue

The Examiner rejected claims 1, 3-6, and 25 under 35 U.S.C. § 103(a) as obvious over Huang, Hoofnagle, and Moody (Ans. 5-7).

The Examiner finds that "Huang et al. teach a method of treating humans infected with hepatitis B comprising administering a combination of interferon-α and thymosin" (Ans. 5). The Examiner finds that "Hoofnagle et al. teach a method of treating humans infected with hepatitis C comprising administering two to five million units of recombinant interferon-α" (Ans. 6). The Examiner finds that "Moody et al. teach an immunopotentiating effect of thymosin-α administered concurrently with chemotherapy in treatment of various cancers, thymosin-α enhances the growth and differentiation of T cells" (Ans. 6). The Examiner concludes that it would have been obvious "to modify the method of Hoofnagle to add thymosin-α to treat hepatitis C infection because Huang et al. have shown that thymosin

strengthens the antiviral effect of interferon-α by inducing production of interferon and by generating active immune T cells" (Ans. 6-7).

Appellant argues that "Hepatitis B and Hepatitis C are different diseases. A treatment for one virus would not be expected to be effective against the other virus. Hepatitis C is caused by an RNA virus and Hepatitis B is caused by a DNA virus" (Reply Br. 2). Appellant argues that Hoofnagle does not "mention of the use of thymosin for treating Hepatitis C or the combination of α-interferon with thymosin for treating Hepatitis C" (App. Br. 11). Appellant argues that "Moody is directed to compositions and methods for treating small cell and non- small cell lung cancers, not viruses, not Hepatitis C virus. Moody indicates that thymosin and interferon operate[] to treat the endogenous biochemical factors that regulate the growth of lung cancer cells" (App. Br. 11).

Appellant argues that "[i]t was not known at the time of the invention whether α-interferon in combination with thymosin α would have the same effectiveness in treating Hep C as they had in treating Hep B. It was not predictable or obvious to try because of the fear of side effects and canceling of one drug by the other" (App. Br. 12).

In view of these conflicting positions, we frame the obviousness issue before us as follows:

Has Appellant demonstrated that the Examiner erred in finding it obvious to treat Hepatitis C with a combination of α-interferon and thymosin α?

Findings of Fact (FF)

1. The Specification teaches that "[t]he interferons are host proteins made in response to viral infections as well as other antigenic stimuli" (Spec. 3, ll. 18-20).

2. Hoofnagle teaches that "Hepatitis C resembles other forms of viral hepatitis clinically" (Hoofnagle 259, col. 1).

3. Hoofnagle teaches that "[b]ecause of the marked effects of alpha interferon therapy in chronic hepatitis B, pilot studies were started using this agent in chronic hepatitis C" (Hoofnagle 260, col. 1).

4. Hoofnagle teaches that the "results from this pilot study were encouraging" and that "a majority of patients with chronic hepatitis C respond to interferon therapy with an improvement both in serum aminotransferase activities and in histologic evidence of disease activity" (Hoofnagle 260, col. 2).

5. Huang teaches that "follow-up observations during one-half to 2 years were performed on 20 patients with chronic hepatitis B who had been treated by combining a small dosage of interferon with thymosin" (Huang translation 2).

6. Huang teaches that the "antiviral effect of [the] combined treatment was prominent in the contrast group" with 61.1 % success in the treated group and 20% success in the "contrast" or control group, so the "effect rate between the two groups was remarkably different ($p<0.01$)" (Huang translation 2).

7. Huang teaches that the "results of the recent and follow-up period showed that the combined treatment of [a] small dosage of interferon

and thymosin was safe and effective. The combined treatment strengthens the antiviral effect, and should be further studied" (Huang translation 2).

8. Moody teaches that "THNα1 and its C-terminal . . . and N-terminal . . . fragments inhibit lung cancer growth in vivo in tumors of both SCLC and NSCLC types of lung cancer cells. No toxic side effects were observed" (Moody, col. 6, ll. 17-21).

Principles of Law

The question of obviousness is resolved on the basis of underlying factual determinations including: (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; (3) the differences between the claimed invention and the prior art; and (4) secondary considerations of nonobviousness, if any. *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966). The Supreme Court has emphasized that "the [obviousness] analysis need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." *KSR Int'l v. Teleflex Inc.*, 550 U.S. 398, 418 (2007).

In *Kubin*, the court commented that "[r]esponding to concerns about uncertainty in the prior art influencing the purported success of the claimed combination, this court [in *O'Farrell*] stated: '[o]bviousness does not require absolute predictability of success … all that is required is a reasonable expectation of success.'" *In re Kubin*, 561 F.3d 1351, 1360 (Fed. Cir. 2009) (*citing In re O'Farrell*, 853 F.2d 894, 903-904 (Fed. Cir. 1988)).

Analysis

Hoofnagle teaches that "Hepatitis C resembles other forms of viral hepatitis clinically" (Hoofnagle 259, col. 1; FF 2). Hoofnagle further teaches that "[b]ecause of the marked effects of alpha interferon therapy in chronic hepatitis B, pilot studies were started using this agent in chronic hepatitis C" (Hoofnagle 260, col. 1; FF 3).

Huang teaches that for Hepatitis B "the combined treatment of a small dosage of interferon and thymosin was safe and effective. The combined treatment strengthens the antiviral effect, and should be further studied" (Huang translation 2; FF 7). Moody teaches that regarding treatment with thymosin, "[n]o toxic side effects were observed" (Moody, col. 6, ll. 17-21). After weighing the totality of the record regarding obviousness, we agree with the Examiner that a preponderance of the evidence supports a determination that the claimed invention is obvious over the prior art. In *KSR*, the Supreme Court stated that an invention may be found obvious if it would have been obvious to an ordinary artisan to try a course of conduct:

> When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103.

KSR, 550 U.S. at 421.

Hoofnagle demonstrates that the ordinary skilled practitioner would routinely apply Hepatitis B treatment methods to the treatment of Hepatitis

C, specifically teaching since interferon-α was successfully used to treat Hepatitis B, it was applied to the treatment of Hepatitis C (FF 3). The ordinary practitioner, familiar with the prior art of Huang and Hoofnagle, would recognize that it would have been obvious to try treatment of Hepatitis C with interferon-α as expressly taught by Hoofnagle in combination with thymosin since the combination was taught to successfully treat Hepatitis B by Huang (FF 5-7).

Application of thymosin, a known compound which enhanced the antiviral effect of interferon-α on Hepatitis B as taught by Huang (FF 5-7), to treat Hepatitis C, represents a situation where the prior art identifies parameters which are critical in the treatment of Hepatitis, and provides guidance as to a combination therapy which may be successful. This also does not represent a situation where the prior art only provides a "general approach", since the prior art provides sufficient specificity to demonstrate that thymosin strengthens the antiviral effect (FF 7) and does not have toxic side effects (FF 8). *See In re Kubin*, 561 F.3d 1351, 1359 (Fed. Cir. 2009). *Also see In re O'Farrell*, 853 F.2d 894, 903 (Fed.Cir.1988).

We are not persuaded by Appellant's argument that "Hepatitis B and Hepatitis C are different diseases. A treatment for one virus would not be expected to be effective against the other virus. Hepatitis C is caused by an RNA virus and Hepatitis B is caused by a DNA virus" (Reply Br. 2)." In fact, the prior art of Hoofnagle expressly demonstrates that because interferon-α was successful in the treatment of Hepatitis B, pilot studies were started using interferon-α for the treatment of Hepatitis C (FF 3). This

demonstrates that the ordinary practitioner would have reasonably expected the Hepatitis B treatment to be effective for Hepatitis C.

Further, Hoofnagle demonstrates that the prior art was aware that for interferon-α, this expectation was fulfilled, since the pilot studies with interferon-α showed response to the therapy (FF 4). We agree with the Examiner that it would have been reasonable to expect the same result with interferon-α combined with thymosin (*see* Ans. 8-9).

We also are not persuaded by Appellant's argument that the "[i]t was not known at the time of the invention whether α-interferon in combination with thymosin α would have the same effectiveness in treating Hep C as they had in treating Hep B. It was not predictable or obvious to try because of the fear of side effects and canceling of one drug by the other" (App. Br. 12). Having found above that the prior art suggests that interferon-α combined with thymosin was used for treatment of Hepatitis B and that interferon-α was used for treatment of Hepatitis C (FF 2-7), it is at least "obvious to try" the combination interferon-α in the treatment of Hepatitis C.

We conclude that there would have been a "reasonable expectation of success" in applying a known drug combination to Hepatitis C, since it was known that Hepatitis C responded to interferon-α, one of the drugs in the combination (FF 2-3) and since it was known that the "combined treatment strengthens the antiviral effect" (Huang translation 2; FF 7). *See In re O'Farrell*, 853 F.2d 894, 903 (Fed.Cir.1988) ("Obviousness does not require absolute predictability of success. Indeed, for many inventions that seem

quite obvious, there is no absolute predictability of success until the invention is reduced to practice.")

We have considered the Sherman Declaration regarding Appellant's argument that "[u]nexpected results have been shown by Applicant" (App. Br. 12). The Sherman Declaration demonstrates that the combination of interferon and thymosin reduced viral titer as compared to interferon alone (Sherman Dec. 4-5). However, the Declaration never states that this result was unexpected (*see* Sherman Dec.). Further, based upon the prior art teaching of Huang that the "combined treatment strengthens the antiviral effect" (Huang translation 2; FF 7), there is evidence that such improved results from the combination would have been reasonably expected by the skilled worker, not an unexpected result. Additionally, since Moody teaches that "[n]o toxic side effects were observed" (Moody, col. 6, ll. 17-21; FF 8), the absence of significant side effects is also not an unexpected result, but rather the expected result.

Conclusion of Law

Appellant has not demonstrated that the Examiner erred in finding it obvious to treat Hepatitis C with a combination of α-interferon and thymosin α.

SUMMARY

In summary, we affirm the rejection of claim 1 under 35 U.S.C. § 103(a) over Huang, Hoofnagle, and Moody. Pursuant to 37 C.F.R. § 41.37(c)(1)(vii)(2006), we also affirm the rejection of claims 3-6 and 25 as these claims were not argued separately.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a)(1)(iv)(2006).

AFFIRMED

dm

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